REMARKS

This is responsive to the final Office Action mailed on March 29, 2006. Applicant has amended claims 1, 8, 10, 44 and 45. Support for the amendment to the claims to add "increased relative to a predetermined value" is provided throughout the specification, for example, at page 3, lines 18-19 and page 9, line 21. Support for the amendment of the claims to insert "regression, progression or onset" in place of "stage" is found in the application, for example, at page 2, lines 27-28 and page 3, lines 3-4 of the application. No new matter has been added.

Claim Objections

The Examiner objected to claims 8, 10 and 42-48 because the recitation of "polypeptide" and "peptide" in parts (iii) and (iv) of claim 8 did not make reference to which other part of the claim was antecedent to these recitations. Applicant has amended claim 8 to provide the appropriate reference in part (iii) and has deleted part (iv) of the claim. Reconsideration of the objection is respectfully requested.

Rejections Under 35 U.S.C. 112, First Paragraph – Enablement

1. The Examiner rejected claims 8 and 10 as lacking enablement for monitoring an antibody. Applicant respectfully disagrees, but to facilitate allowance of the application has amended claims 8 and 10 to remove the recitation of antibody and polypeptide or peptide that binds the antibody, respectively. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

2. The Examiner rejected claims 1, 6-8, 10 and 37-48 as lacking enablement for methods of assessing aberrant expression of Fit-1/ST2 molecules. Applicant respectfully disagrees, but to facilitate allowance of the application has amended the claims to amend the recitation of "aberrant" to "increased relative to a predetermined value". Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

3. The Examiner rejected claims 8, 10 and 42-48 as lacking enablement for the recitation of "determining the stage" of a cardiovascular condition. Applicant respectfully disagrees, but to facilitate allowance of the application has amended the claims to recite determination of "regression, progression or onset" in place of "stage".

Monitoring Fit-1/ST2 expression for determining regression, progression or onset of cardiovascular conditions is enabled by the teachings of the specification. For example, the in vivo studies described on page 68 describe differences in Fit-1/ST2 expression over time as the cardiovascular condition changes with time. Based on such guidance and the high level of skill in the art, the skilled person would be enabled to practice the invention as claimed.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

4. The Examiner rejected claims 1, 6-8 and 10 as lacking enablement for the recitation of detecting Fit-1/ST2 in a biological sample. Applicant respectfully traverses the rejection.

Applicant asserts that the specification enables detection of Fit-1/ST2 in essentially any biological sample. Enablement is evaluated in view of the knowledge and skill of the person of ordinary skill in the art. Put another way, the specification must teach the person of ordinary skill how to make and use the claimed invention, but need not teach that which is already known by the skilled person. It is Applicant's position that the teachings in the specification combined with the skilled person's knowledge is sufficient to practice the claimed invention.

As one example of detecting proteins in biological samples other than blood and serum, many examples of detecting proteins in urine are known to the skilled person. A recent and relevant example of this is the report by Ng et al. on the detection of the cardiovascular disease marker N-terminal pro-brain natriuretic peptide (NT-BNP) in urine (Clinical Sci 106:129-133, 2004). Analysis of NT-BNP was demonstrated in urine, and was found to be equivalent in diagnostic accuracy to analysis of plasma NT-BNP. Therefore, one of ordinary skill in the art is familiar with detection of proteins in urine, and as demonstrated by the Ng et al reference, detection of proteins for the purpose of diagnosing cardiovascular disease can be performed routinely and successfully. Thus, detection of Fit-1/ST2 in patient samples other than blood, plasma and cardiovascular tissue is enabled by the specification.

Detection of proteins larger than Fit-1/ST2 are known in the art. For example, it is known that the larger protein thrombomodulin (575 AA, serum antigens of 105, 52, 46, 31, and 28 kDa) can be detected in blood/serum and urine. See Nakano et al., Thromb Res. 2000 Jul 1;99(1):83-91, Hanyu et al., Clin Rheumatol. 1999;18(5):385-9 and Nakano et al., Thromb Haemost. 1998 Feb;79(2):331-7. This provides a reasonable expectation that a protein the size of Fit-1/ST2 would be measurable in urine.

Furthermore, the expression of ST2 in many tissues of mice has been demonstrated following induction of a cardiovascular condition. See Circulation 2002, 106(23):2961-6, which, although it is a post-filing reference, demonstrates that the well-known technique of RT-PCR can be used to detect Fit-1/ST2 in a variety of biological samples, including left ventricular tissue, thymus, spleen, lung, atrium and liver.

Thus it is readily apparent that the teaching of the specification combined with the knowledge of the person of skill in the art is more than adequate to permit the skilled person to practice the claimed invention without undue experimentation. Accordingly, reconsideration of the rejection is respectfully requested.

5. The Examiner rejected claims 10, 39, 45 and 46 as lacking enablement for the recitation of nucleic acid hybridization other than with full length Fit-1/ST2 nucleic acid molecules. Applicant respectfully traverses the rejection.

The Examiner indicated that the specification does not teach how to diagnose a cardiovascular disease by hybridization of any nucleic acid molecule other than full length Fit-1/ST2, and that it would require undue experimentation for the skilled person to correlate cardiovascular disease with hybridization of the group of possible hybridizing nucleic acid molecules.

Applicant maintains that the person of ordinary skill in the art would not be required to practice undue experimentation for the following reasons. First, the specification teaches the skilled person that aberrant expression of Fit-ST2 is indicative of cardiovascular disease. Second, the skilled person is highly familiar with carrying out hybridization experiments to determine the expression of a given nucleic acid molecule. Third, as noted in the previous amendment, the sequence of many Fit-1/ST2 nucleic acid molecules were known in the art; therefore it would have

been entirely routine for a person skilled in the art to select or design a probe based on the known Fit-1/ST2 nucleic acids to determine expression of Fit-1/ST2. None of the foregoing represents undue experimentation for one of ordinary skill in the art.

The Examiner's comment that one of "ordinary skill in the art would not be able to predict how to diagnose a cardiovascular disease by hybridization of any nucleic acid molecule other than full-length Fit-1" (Office Action at page 6) does not square with the nature of hybridization technology and the level and knowledge of the skilled person. In fact, it would be more likely than not that the skilled person would use a Fit-1/ST2 nucleic acid of less than full length. Even if any experimentation is required to conduct such experiments, it would undoubtedly be routine.

The specification additionally provides guidance for the use of non-full-length nucleic acid probes to determine the expression of Fit-1/ST2 nucleic acids. For example, support is provided for the use of oligonucleotide probes (including microarrays and PCR) and larger hybridization probes (including northern blotting) on the specification on page 12, line 8 to page 13, line 3; page 62 (Example 1, Transcriptional Profiling and Northern Analysis); and page 67 (Example 2). In this regard, it should be recognized by the Examiner that one large category of Fit-1/ST2 nucleic acids that can be used in hybridization-based assays of Fit-1/ST2 expression is primers used in PCR amplification. Selection and use of such non-full-length Fit-1/ST2 nucleic acids is entirely routine in the art.

In view of the guidance provided in the specification, the presence of working examples showing the use of varied probe sizes and hybridization methods, and the knowledge and skill of the person of ordinary skill in the art, Applicant maintains that the invention as claimed is fully enabled. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Rejections Under 35 U.S.C. 112, First Paragraph – Written Description

The Examiner rejected claims 10, 39 and 44-45 under 35 U.S.C. 112, first paragraph, as allegedly lacking an adequate written description. Applicant respectfully traverses the rejection.

The Examiner indicated that the claims read on any size nucleic acid molecule, regardless of size, that is capable of hybridizing to Fit-1/ST2 nucleic acids. The Examiner alleges that Applicant "has not fully defined the genus of nucleic acid molecules that are capable of

hybridizing to Fit-1 and whose hybridization to Fit-1 is diagnostic of cardiovascular disease." (Office Action at page 7). Applicant respectfully disagrees with each of these assertions.

First, the claimed invention is methods for diagnosing a cardiovascular condition using Fit-1/ST2 sequences. The claims are not directed to the sequences *per se*.

Second, Fit-1/ST2 nucleic acids were well known in the art at the time that the application was filed as was detailed in the previous amendment filed by Applicant. Thus, the skilled person readily would have been able to recognize that Applicant invented the claimed methods using the Fit-1/ST2 sequences.

As noted above in response to the enablement rejection, the specification provides descriptive guidance and provides working examples in which nucleic acid probes of varied sizes and composition are used. As will be recognized by the skilled person, the specific hybridization probe used to determine the expression of Fit-1/ST2 does not matter. The application makes it abundantly clear that Applicant's invention involves the recognition that Fit-1/ST2 expression is diagnostic for cardiovascular conditions. It would be equally clear to the person of skill in the art that Applicant was in possession of the invention as now claimed.

Accordingly, Applicant respectfully requests that the rejection of the claims as lacking written description be withdrawn.

Rejections Under 35 U.S.C. 112, Second Paragraph

The Examiner rejected claims 1, 6-8, 10 and 37-48 under 35 U.S.C. 112, second paragraph, as incomplete for omitting method steps (see page 8 of Office Action). Applicant respectfully traverses the rejection.

The Examiner indicated that the person of ordinary skill in the art would not be able to determine if Fit-1/ST2 is increased unless that person knows what constitutes a baseline of Fit-1/ST2 expression, or unless multiple determinations of Fit-1/ST2 are made. (Office Action at page 8).

The claims as now pending recite that Fit-1/ST2 expression that is increased relative to a predetermined value is diagnostic of cardiovascular disease. The skilled person certainly will be able to know if the expression is increased relative to a predetermined value. Therefore, the method does not omit any essential method steps.

In contrast, the Examiner's suggested amendment would add non-essential method steps. That is, practice of the claimed method does not require measuring Fit-1/ST2 expression at two or more time points. As will be apparent to one of ordinary skill in the art, the ordinary practice of the claimed methods in clinical settings will not necessarily involve taking multiple measurements of Fit-1/ST2 expression. To restrict the claims in this manner is not reflective of Applicant's inventive contributions.

Based on these arguments and claim amendments, Applicant respectfully requests reconsideration and withdrawal of the rejection made under 35 U.S.C. 112, second paragraph.

Double Patenting

The Examiner provisionally rejected claims 1, 6-8, 10 and 37-48 under the judicially-created doctrine of obviousness-type double patenting over claims 1-3, 7-11 of copending application serial number 10/435,482. Applicant respectfully traverses the rejection.

According to MPEP § 804 I. B., if the current claims are otherwise allowable, then the provisional double patenting rejection should be withdrawn. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection.

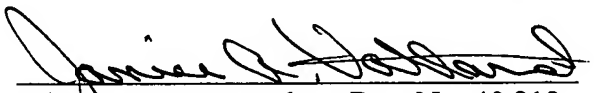
CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

LEE, Applicant



John R. Van Amsterdam, Reg. No. 40,212
Janice A. Vatland, Reg. No. 52,318
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
(617) 646-8000

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